510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:
K040008

B. Purpose for Submission:
Modified product

C. Analyte:
pH and volatile amines

D. Type of Test:
Qualitative colorimetric assay

E. Applicant:
Quidel Corporation

F. Proprietary and Established Names:
QuickVue Advance pH and Amines gII Test

G. Regulatory Information:

1. Regulation section:
   21 CFR §862.1550 Urinary pH (nonquantitative) test system
2. Classification:
   Class 1
3. Product Code:
   CEN
4. Panel:
   Chemistry (75)

H. Intended Use:

1. Intended use(s):
   The test contains two colorimetric qualitative tests for use in the characterization of vaginal fluid samples: 1) a pH test that differentiates vaginal fluid pH < 4.7 from vaginal fluid pH ≥ 4.7; and 2) a test that detects elevated levels of volatile amines (> 0.5 mM trimethylamine) in vaginal fluid.
2. Indication(s) for use:
   "The QuickVue Advance pH and Amines gII test contains two colorimetric tests intended for the qualitative detection of elevated vaginal fluid ph (pH ≥ 4.7) and the presence of volatile vaginal fluid amines. The test is intended for use by health care professionals as an aid in the diagnosis of bacterial vaginosis."
3. Special condition for use statement(s):
   The product is intended for use in a health-care setting.
4. Special instrument Requirements:
   None.

I. Device Description:
The device is a hand-held card with two defined test areas that contain colorimetric indicators that change color when in contact with undiluted vaginal fluid. It detects

vaginal pH ≥ 4.7 and volatile amines at concentrations > 0.5 mM. The pH test is run by gently rubbing a sterile amine-controlled swab over the entire surface of the pH test area. The amine test is run second using the same swab, by gently rubbing from the outside of the test circle to the center. Results for both tests should be run after one minute.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   FemExam TestCard Test
2. Predicate K number(s):
   K962718
3. Comparison with predicate:

   The device is similar to the predicate in the following ways: they have the same intended use and sensitivity, use the same test indicators, use the same test format, use the same clinical sample, and have the same number of steps in the procedure (two - one per test).

   The differences between the tests are: the proposed test is read one minute after application of the sample while the predicate test is read two minutes after application, and the procedural controls and positive indicators are a different shape and color than the predicate.

K. Standard/Guidance Document Referenced (if applicable):

Criteria	Reference:
Precision	NCCLS EP5-T2: Precision performance of clinical chemistry devices- second edition: tentative guideline (1992)
Amsel criteria for diagnosis of bacterial vaginosis	Amsel R, PA Totten, CA Spiegel, KC Chen, D Eschenbach, KK Holmes. 1983. Nonspecific vaginitis. Diagnostic criteria and microbial and epidemiologic associations. Am J Med. 74:14.
Nugent Gram Stain method and interpretation	Nugent R., MJ Krohn , SL Miller. 1991. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of Gram stain interpretation. J. Clin. Microbiology 29:297
Normal vaginal pH levels	Nyirjesy P. 2001. Chronic vulvovaginal candidiasis. Am. Fam. Physician 63:697
Normal vaginal amine levels	Wolrath H, U Forsum, PG Larsson, H Borén. 2001. Analysis of bacterial vaginosis-related amines in vaginal fluid by gas chromatography and mass spectrometry. J. Clin. Microbiology 39:4026

L. Test Principle:

Both the pH and amine test rely on colorimetric pH indicators that produce a visual color change within one minute of sample application. The pH test utilizes the indicator nitrazine yellow. When the pH test area comes in contact with a vaginal fluid sample with a pH≥ 4.7, a distinct greenish-blue plus sign appears against a

yellow background, along with a greenish-blue procedural dot. When the vaginal fluid pH<4.7 only the procedural dot appears against the yellow background. Bromocresol green and an alkali ink containing sodium aluminate are utilized in the amine test. The test area produces a distinct greenish-blue plus sign and a greenish-blue procedural dot against a yellow background when vaginal fluids containing volatile amines at concentrations above 0.5 mM are present. Only the procedural dot appears when volatile amines are not present. In all cases, if the procedural dot does not appear the test is not valid.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The analytical precision of the QuickVue Advance was established by a range of prepared solutions (listed in table) to represent samples. One operator used ten replicates of one lot of Advance reagents at each level. The test was interpreted at one minute and quantified using an internal color score chart where a score of 0.5 is the minimum color intensity for a clearly visible positive test and where 0 and 0.25 are negative. Inter-assay variation was tested as above over 4 days.

Intra-Assay Precision: QuickVue Advance pH Test

pH Standards	Average Color Score	Standard Deviation	% CV	Minimum Test Score	Maximum Color Score
4.0	0	0	N/A	0	0
4.4	0.15	0.13	86%	0	0.25
4.8	1.08	0.24	22%	0.75	1.5
5.5	4.10	0.32	8%	4	5

Intra-Assay Precision: QuickVue Advance Amines Test

Amine Standards	Average Color Score	Standard Deviation	% CV	Minimum Test Score	Maximum Color Score
0 mM	0.10	0.13	129%	0	0.25
0.25 mM	0.25	0.00	0%	0.25	0.25
0.50 mM	0.50	0.00	0%	0.50	0.50
1.00 mM	0.88	0.13	15%	0.75	1.00

Inter-assay Precision: QuickVue Advance pH Test

	Average Color Score (n=10)				Precision		
pH Standards	Day 1	Day 2	Day 3	Day 4	Mean	Std Dev	%CV
4.0	0	0	0	0	0	0	---
4.4	0.15	0.18	0.23	0.28	0.21	0.06	27%

	Average Color Score (n=10)				Precision		
pH Standards	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Mean**	**Std Dev**	**%CV**
4.8	1.08	1.65	1.55	1.45	1.43	0.25	18%
5.5	4.10	4.30	4.00	4.00	4.10	0.14	3%
				Inter-Assay Variation: 16.0%			

Inter-assay Precision: QuickVue Advance Amines Test

	Average Color Score (n=10)				Precision		
Amines Standards	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Mean**	**Std Dev**	**%CV**
0 mM	0.10	0.13	0.05	0.03	0.08	0.05	61%
0.25 mM	0.25	0.25	0.23	0.23	0.24	0.01	6%
0.50 mM	0.50	0.50	0.50	0.50	0.50	0	0%
1.00 mM	0.88	0.88	0.90	0.93	0.89	0.02	3%
					Inter-Assay Variation: 17.5%		

b. Linearity/assay reportable range:
Not applicable, test as used clinically is qualitative.

c. Traceability (controls, calibrators, or method):
Not applicable.

d. Detection limit:
Limits of detection were determined by prepared solutions spanning negative through borderline threshold through low positive; levels tested are in the tables below. Twenty-one (21) replicates of each level were evaluated using three different lots of QuickVue Advance tests. Relative color scores were determined using an internal color score chart where a score of 0.5 is the minimum color intensity for a clearly visible positive test. Data is represented here qualitatively.

Limits of Detection: QuickVue Advance pH Study

	Lot 1		Lot 2		Lot 3	
pH Level	**Correct Call**	**% Correct**	**Correct Call**	**% Correct**	**Correct Call**	**% Correct**
4.0	Neg	100	Neg	100	Neg	100
4.1	Neg	100	Neg	100	Neg	100
4.2	Neg	100	Neg	100	Neg	100
4.3	Neg	100	Neg	100	Neg	100
4.4	Neg	100	Neg	100	Neg	100
4.5	Neg	81	Neg	100	Neg	62
4.6	Neg	48	Neg	52	Neg	38
4.7	Pos	100	Pos	76	Pos	90
4.8	Pos	100	Pos	95	Pos	100
4.9	Pos	100	Pos	100	Pos	100

	Lot 1		Lot 2		Lot 3	
pH Level	**Correct Call**	**% Correct**	**Correct Call**	**% Correct**	**Correct Call**	**% Correct**
5.0	Pos	100	Pos	100	Pos	100
5.5	Pos	100	Pos	100	Pos	100

Limits of Detection: QuickVue Advance Amine Study

	Lot 1		Lot 2		Lot 3	
Amines Level	**Correct Call**	**% Correct**	**Correct Call**	**% Correct**	**Correct Call**	**% Correct**
0 mM	Neg	100	Neg	100	Neg	100
0.25 mM	Neg	86	Neg	86	Neg	95
0.35 mM	Neg	43	Neg	71	Neg	91
0.50 mM	Pos	100	Pos	100	Pos	95
0.75 mM	Pos	100	Pos	100	Pos	100
1.0 mM	Pos	100	Pos	100	Pos	100
2.0 mM	Pos	100	Pos	100	Pos	100
5.0 mM	Pos	100	Pos	100	Pos	100

Referencing NCCLS EP5-T2 guidelines, the sponsor established the limit of detection at pH4.7 and amines at 0.50 mM.

e. Analytical specificity:

To test the specificity of the QuickVue Advance pH and amine test, a variety of over-the-counter vaginal-use products were tested for their ability to interfere with the tests. Negative and positive control solutions were spiked with various concentrations of product; none of the products tested at the concentrations indicated interfered with detection of positives or negative control sample:

QuickVue Advance pH test Interference Study

Substance	**Negative Control**				**Positive Control**			
	Highest Conc Tested w/ No Interference	**Number Correct Calls**			Highest Conc Tested w/ No Interference	**Number Correct Calls**		
		Call	n	%		Call	N	%
None	N/A	Neg	2/2	100%	N/A	Pos	2/2	100%
K-Y Jelly	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Replens	20% w/v	Neg	2/2	100%	4% w/v	Pos	2/2	100%
Delfen	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Conceptrol	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Gyne-Lotrim-3	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Vagistat-1	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Massengil	2% w/v	Neg	2/2	100%	0.2% w/v	Pos	2/2	100%

Substance	Negative Control				Positive Control			
	Highest Conc Tested w/ No Interference	Number Correct Calls			Highest Conc Tested w/ No Interference	Number Correct Calls		
		Call	n	%		Call	N	%
Summer's Eve	20% w/v	Neg	2/2	100%	0.2% w/v	Pos	2/2	100%
Vagisil	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Vaginex	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Vagisil Powder	4% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%

QuickVue Advance Amine test Interference Study

Substance	Negative Control				Positive Control			
	Highest Conc Tested w/ No Interference	Number Correct Calls			Highest Conc Tested w/ No Interference	Number Correct Calls		
		Call	n	%		Call	N	%
None	N/A	Neg	2/2	100%	N/A	Pos	2/2	100%
K-Y Jelly	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Replens	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Delfen	0.1% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Conceptrol	0.4% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Gyne-Lotrim-3	4% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Vagistat-1	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Massengil	0.2% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Summer's Eve	0.02% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Vagisil	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Vaginex	20% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%
Vagisil Powder	4% w/v	Neg	2/2	100%	20% w/v	Pos	2/2	100%

f. Assay cut-off:
The sponsor-identified levels of the assay are a pH 4.7 and an amine concentration of 0.50 mM. These levels correspond to two of the four Amsel criteria, a well-recognized method for diagnosing bacterial vaginosis (see reference above). The Amsel criterion for pH is ≥4.7 while the criterion for amines is the detection of a 'fishy' amines odor when a drop of 10% KOH is added to a sample of vaginal fluid (the "whiff test").

2. Comparison studies:
   a. Method comparison with predicate device:
   Not performed; device was compared to clinically based standard criteria (see below).
   b. Matrix comparison:
   Not applicable.

3. Clinical studies:
   A multi-center study established the clinical performance of the device. A total of 464 vaginal fluid samples were collected from post-pubertal women. Approximately 43% of the women had signs or symptoms associated with

altered vaginal pH and elevated amines. Vaginal fluid was first sampled for the QuickVue Advance tests then sampled for Amsel analysis and Nugent Gram stain assessment.

For a given patient to be considered positive by the Amsel criteria, she had to have 3 of 4 clinical criteria present: elevated pH, detectable volatile amines, 'clue' cells present on microscopic evaluation, and appearance (color, consistency, and amount) of vaginal discharge. To be considered 'positive' by QuickVue Advance in the clinical studies described below, the patient had to have a positive pH test and a positive amines test.

Of the 464 specimens, 302 patients were negative and 162 were positive by the Amsel criteria. The table below presents a comparison of the QuickVue Advance test to the Amsel criteria:

QuickVue Advance Clinical Performance Comparison to Amsel Criteria

Comparative Method		**Amsel Reference Criteria**	
	Outcome	Positive	Negative
Quidel Advance pH and Amines	Positive	140	24
	Negative	13	287

Discordant results were reconciled using Nugent Gram Stain method; a score of 7 or more was considered positive for bacterial vaginosis:

QuickVue Advance Clinical Performance Comparison to Amsel Criteria Reconciled by Nugent Gram Stain

Comparative Method		**Amsel Reference Criteria**	
	Outcome	Positive	Negative
Quidel Advance pH and Amines	Positive	149	15
	Negative	13	287

Clinical sensitivity and specificity are shown below:

QuickVue Advance Clinical Performance

	Result	**Unreconciled Clinical Criteria**	**Reconciled Clinical Criteria**
QuickVue Advance Clinical Criteria	**Sensitivity**	91.5%	92.0%
	Specificity	92.3 %	95.0%
	Overall	*92.0%*	*94.0 %*

In an evaluation of the test in three physician's office laboratories, various operators assessed coded, known specimens over three days with the following results:

Summary of Physician's Office Laboratory Studies

Sample	% Correct	n
Negative	97%	107/110
Positive	99%	117/118
Moderate Pos	100 %	120/120
Invalid Result	100 %	4/4
Overall	*99 %*	*348/352*

According to the Flesh-Kincaid Grade-Level index, readability of the package insert was Grade 7.6.

4. Clinical cut-off:
   The sponsor's determination of a vaginal pH cut-off is based on the Amsel criteria (reference above). The cut-off level for amines is based on studies done to support the predicate device. Vaginal fluid samples from 'whiff test' positive women were tested, and around 90% had amine levels above 0.5 mM.

5. Expected values/Reference range:
   Normal vaginal fluid pH is typically 3.8 to 4.5 from although there is individual variation even in healthy women. Pregnancy, menopause, and other health conditions may change vaginal pH. Amines are usually not detectable, or are present at very low concentrations.

N. Conclusion:

The submitted information in this pre-market notification is complete and supports a substantial equivalence decision.